Modern Concepts of Cardiovascular Disease

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VIRUS MYOCARDITIS

Myocarditis in the various acute bacterial diseases has been repeatedly stressed during the last few years. The clinician less frequently than the pathologist has attempted to explain unusual or fleeting electrocardiographic changes, and, occasionally, unexpected deaths in these diseases on the basis of a true inflammation of the myocardium. The pathologist by painstaking examination of many blocks of the myocardium has found significant changes. During the war, myocarditis was also encountered in a number of Rickettsial diseases, foremost among which was scrub typhus.

Occasional reports of myocardial changes in diseases, now recognized as of viral origin, have appeared in the literature during the past twenty years. More recently, experimental work with various viruses, identification of certain viruses in patients who subsequently died with myocarditis, and electrocardiographic changes in patients with well-known virus disease, have shown conclusively that myocarditis occurs in virus diseases. Myocarditis may be recognized clinically, and may be the cause of death in some of these patients.

Before the era of modern virus studies myocarditis, to which no cause could be attributed, but which now is considered of viral origin, was occasionally encountered in various laboratory animals known to have been well otherwise. It was found in about thirty per cent of one series of Swiss strain mice. Spontaneous (so-called) interstitial myocarditis was described in apparently well dogs. There are a number of reports of myocarditis occurring in animals fed diets which were insufficient in minerals and proteins. It seems possible that myocarditis occurring in these animals may also have been the result of complicating virus disease.

Microscopically, these myocarditides were characterized by infiltration of lymphocytes and endothelial leucocytes; only occasional polymorphonuclear leucocytes, plasma cells, and fibroblasts were present. In some of these animals pleuro-pericardial hemorrhages and testicular hemorrhages were also found.

Helwig and Schmidt were able to isolate a virus from a group of anthropoid apes dying from interstitial myocarditis and were able to produce myocardial lesions consistently in mice. In later reports they maintained to have isolated an agent from a chimpanzee dying of interstitial myocarditis which produced myocarditis and encephalitis in mice and hamsters, and myocarditis in guinea-pigs (virus of "encephalo-myocarditis"). They remarked that the morphologic findings in the heart duplicated, to a remarkable degree, the myocardial lesions found in human heart muscles in several virus diseases. They also ventured that, perhaps, isolated myocarditis of humans (Fiedler's myocarditis) might be caused by a virus. It is interesting that sera from 17 patients who suffered from so-called three day fever, occurring among Army personnel stationed in and near Manila, had appreciable amounts of specific neutralizing antibodies for the encephalo-myocarditis virus.

There are reports indicating that the incidence and severity of myocarditis in rabbits suffering from a variety of viral infections, are markedly increased when these animals are submitted to procedures that tend to decrease the amount of oxygen supplied to the heart.

There are on record electrocardiographic studies of rabbits with induced virus myocarditis (Virus III). During the acute stage the majority of these animals developed histologically demonstrable myocarditis, and after recovery from the infection small scars were found in the myocardium of many. Definite abnormalities in cardiac function, including complete auriculo-ventricular heart block, were demonstrated in the electrocardiogram during the period in which acute myocarditis existed. This association of abnormal electrocardiogram with the structural lesion in the heart led to the conclusion that in this disease of the rabbit disturbed function is caused by actual lesions, and not by the toxicity of the disease.

The intratesticular inoculation of vaccinia, pseudorabies, inflammatory fibroma, strain A fibroma and myxoma viruses into rabbits which had been prepared by a preceding intravenous injection of a solution of acacia, was followed by the appearance of cardiac lesions in the majority of the animals. The reaction in the heart was as a rule typical of the agent causing it. Thus, in the acute exudative lesion of pseudorabies intranuclear inclusion bodies were seen. The myxoma virus induced proliferation of the typical large myxoma cells, and the fibroma virus, the characteristic fibroblasts in the interstitial tissue of the heart muscle. The vaccinia virus produced a less specific picture of muscle necrosis and leucocytic exudation.

Myocarditis in man in various virus diseases is being reported more and more frequently, certainly in sufficient volume to arrest the attention of the practicing physician. In a recent communication it was emphasized that from a clinical point of view importance should be attached to virus myocarditis connected with epidemic infective hepatitis, infectious mononucleosis, yellow fever, varicella, dengue, poliomyelitis, atypical primary pneumonia, rubeola, measles, mumps, and influenza-like infections. It is owing to the benign character of the majority of these diseases that the myocardial involvement is usually overlooked.

Recently, myocarditis has been reported in acute epidemic encephalitis as "nonpurulent myocarditis," where infiltration mainly of lymphocytes and rela-

tively few polymorphonuclear leucocytes were present in the myocardium. Among 17 patients dying from poliomyelitis, myocarditis was encountered in ten. Histologically the inflammatory cells consisted principally of lymphocytes, and neutrophiles, and occasionally diffuse infiltrations of polymorphonuclear leucocytes were noted. Among 35 cases of poliomyelitis in which necropsy was performed, myocarditis was demonstrated in 14. The lesions were classified as severe in six, moderately severe in four, minimal in three, and healed in one. Several lesions were characterized by widespread coagulation necrosis associated with an abundance of inflammatory cells, mainly polymorphonuclear leucocytes, and, to a lesser degree, macrophages and lymphocytes. The cells were found most commonly about necrotic myocardial fibers, but were also noted between seemingly viable muscle bundles and in perivascular regions. Also isolated foci of degenerated muscles were noted. From the evidence on hand, it seemed probable that these lesions were caused by the virus which causes poliomyelitis. Whether or not this assumption is accurate, it is apparent that in cases of poliomyelitis, myocarditis occurs rather frequently. There is more and more evidence accumulating that myocarditis may also be present in various forms of encephalitis. Whether or not it occurs in lymphocytic chorio-meningitis can not be stated at the present time. It has also been reported recently in four patients with Friedreich's ataxia. However, the virus origin of this disease has not been proven.

Non-bacterial myocarditis was also reported in Influenza A virus infection where the virus had been isolated from the lungs. This recalls the fact that circulatory failure had been observed with great frequency during and after the pandemic of 1918. Cardiac disturbances observed after Influenza, such as: bradycardia,, extrasystoles, partial or complete heart block, sinus—nodal block, loss of various complexes, and T wave changes in the electrocardiogram, may be explained on the basis of myocarditis. In two recently reported cases necrosis of muscle fibers was found with extensive infiltration of lymphocytes, plasma cells, large mononuclear cells, and occasional eosinophiles and mast cells. Prolonged and diligent search for evidence of myocardial damage was stressed. Again certain similarities between this type of myocarditis and Fiedler's or isolated myocarditis were pointed out. Myocardial lesions in Psittacosis and primary atypical pneumonia (interstitial pneumonitis) have also been reported. In the latter, clusters of mononuclear cells in the epicardium and distributed around the interstitial capillaries and larger vessels, have been found. It is noteworthy that bradycardia is often observed in atypical pneumonia.

Acute myocarditis with electrocardiographic changes apparent in the terminal deflections of the chest lead has been observed as a sequel of infectious mononucleosis. Also first degree heart block with prolonged PR interval and electrocardiographic tracings indicative of acute myocarditis had been reported previously. A detailed study of infectious mononucleosis conducted in the Armed Forces Institute of Pathology disclosed changes in the myocardium in six out of eight autopsies. Aggregates of lymphocytes were sparsely distributed within the myocardium about small blood vessels. They were also present in small numbers beneath the endocardium. In only one case was the reaction virtually negligible. In another the cellular infiltrate was rather prominent. A few interstitial collections of mononuclear cells and lymphocytes of moderate size were stressed by another investigator.

Myocarditis complicating measles was described a number of years ago. In a relatively recent study of ten hearts, two showed myocardial changes, three showed foci of pericarditis, and five showed no histopathologic changes. Among 91 hearts in another series, four were said to show microscopically more than the usual toxic changes. The cellular infiltrations consisted mainly of lymphocytes.

More recently, electrocardiographic evidence of complete heart block has been observed in two patients with epidemic parotitis (mumps). Among 104 consecutive patients with epidemic parotitis, evidence of myocardial involvement was observed 16 times (15.4 per cent). In all but two patients the electrocardiographic changes were transitory and of short duration.

Myocardial degeneration with only occasional evidence of inflammatory changes often occurs in Yellow Fever. Also in experimentally produced Yellow Fever outspoken myocarditis was observed. From electrocardiographic studies myocardial changes have also been suspected in epidemic hepatitis.

Even old texts of pathology mention the occurrence of myocarditis, in small pox. It is said to occur also in varicella.

It has been stated repeatedly that myocarditis found in virus diseases must not necessarily be caused by that respective virus. However, a number of investigators concluded that from the studies of some viruses it is apparent that the myocardial lesions are due to the actual presence of the virus. Others maintain that it is difficult to assay the importance of virus diseases as the cause of myocarditis, since bacterial infections so often complicate fatal cases. Since it has been shown experimentally that the severity of virus induced myocarditis is markedly increased when the oxygen supply to the heart is decreased, it might very well be that a complicating pneumonia, by decreasing the oxygen supply to the heart, constitutes a factor which makes the virus myocarditis in such patients more severe.

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